

REMARKS

I. Status Summary

Claims 1-19 were filed in the subject application. Election by applicants of Group I, claims 1-17 has previously been acknowledged by the U.S. Patent and Trademark Office (hereinafter "the Patent Office") and claims 1-17 examined. Claims 4 and 11 have previously been cancelled, and claims 18-19 have previously been withdrawn from prosecution. Accordingly, claims 1-3, 5-10, and 12-19 have currently been examined and are pending in the Patent Office.

Claims 1, 2, 9, 16, and 17 presently stand rejected by the Patent Office under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,252,466 to Cronan (hereinafter referred to as "Cronan") in view of U.S. Patent No. 5,283,173 to Fields et al. (hereinafter referred to as "Fields et al.").

The Patent Office has rejected claims 1, 2, 5-9, and 12-16 under 35 U.S.C. §103(a) as allegedly being unpatentable over Cronan in view of Fields et al. and further in view of the journal article to Rigaut et al. (*Nature Biotech*, 17:1030-1032, 1999; hereinafter referred to as "Rigaut et al.").

Claims 1-3, 5-10, and 12-17 presently stand rejected by the Patent Office under 35 U.S.C. §103(a) as allegedly being unpatentable over Cronan in view of Fields et al. in view of Rigaut et al. and further in view of U.S. Patent No. 6,114,111 to Luo et al. (hereinafter referred to as "Luo et al.").

Reconsideration of the application based on the arguments set forth herein is respectfully requested.

II. Response to the Rejections Under 35 U.S.C. §103(a)

A. Cronan in view of Fields et al.

Claims 1, 2, 9, 16, and 17 presently stand rejected by the Patent Office under 35 U.S.C. §103(a) as allegedly being unpatentable over Cronan in view of Fields et al. Particularly, the Patent Office asserts that Cronan teaches every element of the rejected claims, except for identifying any binding partners that bind said protein of interest in said complex. However, the Patent Office asserts that Fields et al.

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teaches a yeast two-hybrid assay for identifying binding partners to a test protein using a library of cDNA plasmids. Accordingly, the Patent Office asserts that it would have been obvious to one of ordinary skill in the art to combine the teachings of Cronan and Fields et al. to arrive at the subject matter of the rejected claims.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants submit that in order to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation in the references themselves to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. Manual of Patent Examining Procedures (M.P.E.P.) 2142; *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Patent Office asserts that Cronan teaches a method for obtaining *in vivo* binding partners of a protein in accordance with the presently claimed subject matter. See, Official Action, page 4, first full paragraph. Applicants respectfully disagree. Rather, the stated objective of Cronan is a method for purifying fusion proteins as set forth in the specification, abstract, and claims of Cronan. Applicants particularly point to column 1, lines 24-28 of Cronan which recite: "...the invention comprises a method of purifying the fusion protein by utilizing binding partners that bind to the fusion protein only after it has been modified by post-translational modification." Accordingly, applicants respectfully submit that by asserting that the disclosure is directed to the purification of the fusion protein, Cronan directly teaches away from a method for *in vivo* isolating and/or screening for binding partners of a protein, as disclosed in independent claims 1, 9, and 16.

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Applicants further assert that the term "binding partner" as used in the specification of the subject application refers to any of a pair of organic chemical moieties which, under physiological conditions, associate non-covalently to form a complex, including for example, receptors and ligands, antigens and antibodies, enzymes and substrates, and so forth. See, for example, page 6, line 31, through page 7, line 4 of the subject application.

In comparison, the term "binding partner" as used in Cronan refers to the entity that binds to the fusion protein tag only after it has been modified. Applicants particularly point to column 5, line 65, through column 6, line 16, which recites:

The modified fusion protein may be purified from mixtures of materials such as cell extracts or the culture medium obtained upon culturing the transformed host by a method comprising: providing a binding partner that binds to the fusion protein only after it has been modified...The binding partner may be antibody or any compound which binds to the fusion protein only after it has been modified. For instance, when the fusion protein is a biotinated protein, the binding partner may be antibody to biotin, but is preferably selected from the group consisting of avidin, streptavidin, and derivatives and analogs thereof.

Accordingly, applicants respectfully submit that "binding partner" as used in Cronan ("...the invention comprises a method of purifying the fusion protein by utilizing binding partners that bind to the fusion protein only after it has been modified by post-translational modification") does not refer to the moieties that associate with the protein of interest, as set forth in independent claims 1, 9, and 16 of the subject application.

As discussed above, applicants respectfully submit Cronan does not teach or suggest methods of isolating and/or screening for binding partners that bind to a protein of interest, as set forth in independent claims 1, 9, and 16 of the subject application. Cronan appears to at best teach methods directed the purification of a fusion protein, not to the purification of the fusion protein and purification and identification of any associated binding partners. Thus, one of ordinary skill in the art relying on the teachings of Cronan would be guided to select the methods disclosed

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therein when attempting to purify only the fusion protein of interest, and would be dissuaded by the teachings of Cronan to identify the moieties that bind to the fusion protein of interest. In fact, Cronan appears to teach away from identifying for binding partners that bind to a protein of interest, as set forth in independent claims 1, 9 and 16 of the subject application.

To elaborate, applicants particularly point to column 15, lines 17-21, which recites (emphasis added):

When a cell extract or cell culture medium is passed over a low affinity monomer avidin column, only the biotinated fusion protein and other biotinated proteins are bound. The bound biotinated proteins are eluted using a biotin-containing buffer.

Accordingly, applicants respectfully submit that Cronan teaches away from methods of identifying for binding partners that bind to a protein of interest. Rather, Cronan appears to teach the isolation of only the fusion protein, or other proteins containing the isolation tag, isolated under conditions such that moieties associated with the fusion protein are not isolated, and do not remain associated with the fusion protein. Thus, applicants respectfully submit Cronan does not teach the identifying for any binding partners that bind the protein of interest within the fusion protein, as recited in independent claims 1, 9, and 16 of the subject application.

Applicants respectfully submit that Fields et al. does not provide for the cited deficiencies of Cronan. Particularly, Fields et al. appears to at best teach methods for detecting protein interaction using the reconstitution of the activity of a transcriptional activator. Fields et al. does not appear to teach utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can be used to identify any binding partners that bind the protein of interest in a co-purified complex. Fields et al. also does not appear to teach introducing into the cell the plurality of potential binding partners. Thus, applicants respectfully submit that Cronan and/or Fields et al., either alone or in combination, do not teach or suggest each and every element of independent claims 1, 9, and 16. Further, applicants respectfully submit

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there is no motivation to combine the teachings of Cronan and Fields et al. Accordingly, applicants submit that the cited combination does not support the instant rejection of independent claims 1, 9, and 16.

Hence, applicants respectfully submit that the instant 35 U.S.C. §103(a) rejection of independent claims 1, 9, and 16 over Cronan in view of Fields et al. has been addressed. Accordingly, applicants respectfully request that the rejection of independent claims 1, 9, and 16 be withdrawn at this time. A Notice of Allowance is also respectfully requested.

Applicants assert that claims 2 and 17 depend from independent claims 1 and 16, respectively. In view of the dependency of these claims, the instant 35 U.S.C. §103(a) rejection of 2 and 17 over Cronan in view of Fields et al. is also believed to have been addressed. Accordingly, applicants respectfully request the instant rejection of claims 2 and 17 be withdrawn at this time. A Notice of Allowance is also respectfully requested.

B. Cronan in view of Fields et al. and Further in view of Rigaut et al.

The Patent Office has rejected claims 1, 2, 5-9, and 12-16 under 35 U.S.C. §103(a) as allegedly being unpatentable over Cronan in view of Fields et al. and further in view of Rigaut et al. Particularly, the Patent Office asserts that the combination of Cronan and Fields et al. teach every element of the rejected claims, except the affinity tagging of the fusion protein, and cleaving the protein of interest from the post-translational modification sequence prior to identifying binding partners of the protein of interest. However, the Patent Office asserts that Rigaut et al. provides for the asserted deficiencies of Cronan and Fields et al.

After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

As previously discussed hereinabove, Cronan and Fields et al., either alone or in combination, are not believed to teach or suggest each and every element of independent claims 1, 9, and/or 16. Applicants respectfully submit Rigaut et al. does

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not cure the above-noted deficiencies. Specifically, Rigaut et al. does not teach a method of utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can be used in identifying for any binding partners that bind the protein of interest in a co-purified complex. Rather, Rigaut et al. appears to at best teach a tag system for protein complex characteristics, limited to yeast studies.

Thus, applicants respectfully submit that Cronan, Fields et al., and Rigaut et al. do not teach or suggest, alone or in combination, each and every element of independent claims 1, 9, and 16. Accordingly, applicants respectfully submit that the instant 35 U.S.C. §103(a) rejection of independent claims 1, 9, and 16 has been addressed. Hence, applicants respectfully request the instant rejection of independent claims 1, 9, and 16 under 35 U.S.C. §103(a) in view of Cronan, Fields et al., and Rigaut et al. be withdrawn at this time. A Notice of Allowance is also respectfully requested.

Claims 2, 5-8 and 12-15 depend directly or indirectly from independent claims 1, 9, or 16. In view of the dependency of these claims, the instant 35 U.S.C. §103(a) rejection of claims 2, 5-8, and 12-15 over Cronan in view of Fields et al. and further in view of Rigaut et al. is also believed to have been addressed. Accordingly, applicants respectfully request the instant rejection of claims 2, 5-8 and 12-15 be withdrawn at this time. A Notice of Allowance is also respectfully requested.

C. Cronan in view of Fields et al. in view of Rigaut et al.
and Further in view of Luo et al.

Claims 1-3, 5-10, and 12-17 have been rejected by the Patent Office under 35 U.S.C. §103(a) as allegedly being unpatentable over Cronan in view of Fields et al. in view of Rigaut et al. and further in view of Luo et al. Particularly, the Patent Office asserts that Cronan in view of Fields et al. in view of Rigaut et al. teach every element of the rejected claims, except for the use of a mammalian host cell. However, the Patent Office asserts that Luo et al. provides for the asserted deficiency.

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After careful consideration of the rejection and the Patent Office's basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

As previously discussed hereinabove, the cited combination of Cronan and Fields et al. and Rigaut et al., either alone or in combination, do not teach or suggest each and every element of any of independent claims 1, 9, and 16. Applicants respectfully submit Luo et al. does not cure the above-noted deficiencies. Specifically, Luo et al. does not teach a method of utilizing a fusion protein comprising a protein of interest and a post-translational modification sequence, which after expression and post-translation modification, can be used in identifying any binding partners that bind the protein of interest in a co-purified complex. Rather, Luo et al. appears to at best teach utilizing two fusion proteins, the first of which contains a DNA binding domain fused to a "bait" protein and the second of which consists of a transcriptional activation domain fused to a "test" protein, to analyze protein-protein interactions.

Thus, applicants respectfully submit that Cronan, Fields et al., Rigaut et al. and Luo et al. do not teach or suggest, alone or in combination, each and every element of independent claims 1, 9, and/or 16. Accordingly, applicants submit that the cited combination does not support the instant rejection of claims 1, 9, and 16. Hence, applicants respectfully submit that the instant 35 U.S.C. §103(a) rejection of claims 1, 9, and 16 has been addressed. Thus, applicants respectfully request the instant rejection of independent claims 1, 9, and 16 be withdrawn at this time. A Notice of Allowance is also respectfully requested.

Applicants assert that claims 2-3, 5-8, 10, 12-15, and 17 depend directly or indirectly from independent claims 1, 9, or 16. In view of the dependency of these claims, the instant 35 U.S.C. §103(a) rejection of 2-3, 5-8, 10, 12-15, and 17 over Cronan in view of Fields et al. in view of Rigaut et al. and further in view of Luo et al. is also believed to have been addressed. Accordingly, applicants respectfully request the instant rejection of claims 2-3, 5-8, 10, 12-15, and 17 be withdrawn at this time. A Notice of Allowance is also respectfully requested.

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CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.


DEPOSIT ACCOUNT

A check in the amount of \$1,520.00 is enclosed. The Commissioner is hereby authorized to charge any other fees associated with the filing of this correspondence to Deposit Account No. 50-0426.

Respectfully submitted,

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Date: March 19, 2007

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